



Declaration of Tonny Jørgensen

For The United States Patent and Trademark Office

Applicants: Weidner, Morten Sloth

Serial no.: 09/613,468

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For: Novel composition containing extracts of *Bytyrospermum parkii* and the use of such a composition for preparing a medicament or a dietary supplement for the treatment or prevention of inflammation, hypersensitivity or pain.

Examiner: Gollamudi, sharmila S

Art unit: 1616

DECLARATION OF TONNY JØRGENSEN

1. I, **TONNY JØRGENSEN**, of Copenhagen, Denmark, an expert within the field of plant extracts and their medical applications do state and declare as follows:
2. I believe that I am a person skilled in the art to which the above-captioned application pertains. Please find attached to this declaration my Curricula Vitae (Appendix B).
3. I have read and understood the pending claims in the application in question as well as the Office Action related thereto dated 12 February 2002 and the cited prior art herein. In respect to this Office Action, I have the following comments:
4. I do consider that Zabotto et al discloses compositions with low content of triterpenes. As can be calculated from claim 1 of Zabotto et al, the cosmetic composition comprises 1 to 80 % w/w of the Karite oil that in turn comprises 1.2 to 1.5 % w/w of unsaponifiable matter. As can be further seen in column 2, lines 36 to 63, the unsaponifiable matter comprises 10-15 % w/w of triterpenic oil, of which α -Amyrin amounts to about 46%, β -Amyrin amounts to about 10%, Butyrospermol amounts to about 26%, and Lupeol amounts to about 16%.

Thus, according to my understanding the cosmetic compositions of Zabotto et al. comprises:

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triterpenic oil (%w/w):	0.001 - 0.180
α -Amyrin (%w/w):	0.0006 - 0.0828
β -Amyrin (%w/w):	0.0001 - 0.0180
Butyrospermol (%w/w):	0.0003 - 0.0468
Lupeol (%w/w):	0.0002 - 0.0288

Compositions of the present invention comprise at least 5% w/w of a triterpene fraction comprising at least 2% w/w Lupeol, at least 2% w/w α -Amyrin and/or β -Amyrin, and at least 2% w/w Butyrospermol. Thus, compositions according to the present invention comprise at least:

triterpenic oil (%w/w):	5
α -Amyrin (%w/w):	0.1
β -Amyrin (%w/w):	0.1
Butyrospermol (%w/w):	0.1
Lupeol (%w/w):	0.1

5. Under my supervision studies have been carried out, which demonstrate that the compositions of the present invention are capable of relieving the symptoms of atopic dermatitis, allergic contact dermatitis and psoriasis upon topical application (see Appendix A, Examples 1-3). Notably, in two cases the persons were in the need of steroids for relieving their symptoms.

6. Moreover, the therapeutic effect in persons suffering from psoriasis and osteoarthritis has been studied upon oral administration of compositions of the invention. As can be seen from Appendix A, Examples 4 and 5, the compositions led to a reduction in the lichenified skin areas and redness seen in persons suffering from psoriasis and led to pain relief in persons suffering from osteoarthritis such that concurrent medication with Ibuprofen is needless.

7. I respectfully disagree with the Examiner's contention that in the light of the teachings of Laur et al it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide such compositions that upon oral or topical administration will result in the anti-inflammatory effect seen in persons experiencing inflammatory diseases (see Appendix A). Notably, such compositions comprise high concentrations of the specific triterpenes, α -amyrin, β -amyrin, butyrospermol and lupeol.

In my opinion, Laur et al. teaches compositions comprising a mixture of fractions rich in unsaponifiable materials obtained from shea butter (see claim 14). As can be seen from Example 5 of Laur et al, the mixtures relates to mixtures of "cold-insoluble fractions" and "hot-insoluble" fractions consisting of sterols, free-fatty acids, aliphatic and triterpene fatty alcohols, triglycerides and very apolar constituents such as karitenes and gum (column 11, lines 46 to 51).

Therefore, Laur et al. does not teach compositions that upon oral or topical administration lead to the anti-inflammatory effects as observed by us. (Appendix A).

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8. Moreover, I respectfully disagree in the Examiner's contention that it would have been obvious to one of ordinary skill in the art at the time the invention was made to apply Zabotto et al.'s karite composition to mucous membranes since the Journal of Pharmacology discloses that shea butter is known to relieve inflammation in the nostrils. In my understanding, the Journal of Pharmacology cites a study investigating the effect of shea butter in comparison to the anti-congestive drug, xylometazoline, and placebo on the relieving effect of the congestion of nostrils. To my best knowledge, the drug Xylometazoline is not recognised as an anti-inflammatory drug, but rather as a drug belonging to the group of drugs with α -adrenomimetic activity that has vaso-constricting properties, for which reason Xylometazoline is well known for its reducing effect on swelling and congestion upon administration to the nasal mucosa. According to the study cited in the Journal of Pharmacology, shea butter has a better effect than Xylometazoline in relieving congestion. Therefore, the skilled person may not expect such an anti-inflammatory effect as observed in the Examples of Appendix A in the light of the combined teachings of Journal of Pharmacology and Zabotto et al.

9. In summary, in light of the present prior art it is not obvious to expect a relieve in the symptoms of anti-inflammatory diseases exemplified by atopic dermatitis, allergic contact dermatitis, psoriasis and osteoarthritis upon administration of compositions comprising high levels of selected triterpenes.

10. For the reasons stated above, I am of the opinion that the invention described by the present application was not obvious to the person skilled in the art.

11. I further declare that all statements made herein of my knowledge are true, and further that the statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardise the validity of the application or any patent issued thereon.

Dated: 9/8-09Signature: 

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Appendix A

Examples on the therapeutic effect of the compositions of the invention.

Compositions (SBE-C50 or SheaNature®) comprising:

triterpenic oil (%w/w):	22
α -Amyrin (%w/w):	9.2
β -Amyrin (%w/w):	1.3
Butyrospermol (%w/w):	0.3
Lupeol (%w/w):	1.2

were evaluated for their therapeutic efficacy in persons suffering from various inflammatory skin diseases (atopic dermatitis, allergic contact dermatitis and psoriasis) or from osteoarthritis.

The improvements in disease symptoms were evaluated subjectively without the supervision of a medical practitioner.

Example 1.

Name of Disease:	Infantile eczema (atopic dermatitis)
Compound Tested	SBE-C50
Prior medication:	Locoid®, 0.1% hydrocortisone.
History:	Girl aged 4 years has occasionally red and soared skin mostly in hollows of elbows and knees.
Trial medication:	Shea butter extract applied topically as an ointment once or twice daily when required. No concurrent treatment with Locoid®.
Subjective Improvements:	After 3-4 days of treatment with the trial medicine, the red areas disappear. No thinning or other kind of skin deformation is observed. The disease returns regularly.
Clinical evaluation:	No clinical evaluation by a physician

Example 2.

Name of Disease:	Osteoarthritis.
Compound Tested	SheaNature®
Prior medication:	Ibuprofen. Arthrotec®, 1 tablet (63.2 mg) twice daily. Panodil® as required.
History:	Woman aged 74 years has had increasing osteoarthritis over the last ten years.
Trial medication:	SheaNature® used as an oral nutritional supplement in a total daily dose of (3 x 2 g) 6 g with the meal morning, lunch, and supper. No concurrent treatment with Ibuprofen was needed.
Subjective Improvements:	After 10 days of treatment with the trial medicine, pain was relieved to the extent that life again became bearable and after five weeks, treatment with Arthrotec® stopped. She still takes Panodil® as required (once or twice weekly).

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Clinical evaluation: No clinical evaluation by a physician

Example 3.

Name of Disease: HLA-B27 positive mediated Psoriasis
 Compound Tested: SheaNature®
 Prior medication: None. Nutritional supplement: 30 ml. fish oil pr. week
 History: Man aged 58 years has had psoriasis from childhood
 Trial medication: SheaNature® used as an oral nutritional supplement in a total daily dose of 6 g. with the meal morning and evening.
 Subjective improvements: After 10 - 14 days of treatment with the trial medicine, a profound reduction in lichenified skin areas and redness was observed
 Clinical evaluation: No clinical evaluation by a physician

Example 4.

Name of Disease: HLA-B27 positive mediated Psoriasis
 Compound Tested: SBE-C35
 Prior medication: None. Nutritional supplement: 30 ml. fish oil pr. week
 History: Man aged 58 years has had psoriasis from childhood
 Trial medication: Shea butter extract applied topically as an ointment once daily after shower
 Subjective improvements: After 7 days of treatment with the trial medicine, a reduction in lichenified skin areas and redness was observed
 Clinical evaluation: No clinical evaluation by a physician

Example 5.

Name of Disease: Allergic contact dermatitis (case).
 Compound Tested: SBE-C50.
 Prior medication: Elocon®. 0.1 % mometasone. Once daily during 2 weeks.
 History: Woman aged 39 years bought a new pair of leather shoes and after almost 2 weeks' usage an acute dermatitis appeared on the instep of both feet. The disease was treated and the skin was restored after 2 months.
 One year after, the shoes were used a couple of hours during two days, and the dermatitis reappeared.
 Trial medication: Shea butter extract applied topically as an ointment once a day for three days. No concurrent medication with Elocon®
 Subjective improvements: After 3 days of treatment with the trial medicine the skin was restored.
 Clinical evaluation: No clinical evaluation by a physician.

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Appendix B

CURRICULUM VITAE

PERSONAL DETAILS:

Address Dalstrøget 94, 1.tv.
DK-2860 Søborg
Date of birth 30.08.1969

PROFESSIONAL EXPERIENCE:

09/2001 -

C.E.O. of BSP Pharma A/S, a joint venture between Astion A/S and Aarhus Oliefabrik A/S.

MAIN RESPONSIBILITIES

- Strategy development and implementation
- Budgeting and Business Administration
- Handling regulatory and legal affairs (e.g. FDA)
- Business Development, commercialisation of projects
- Pharmaceutical and cosmeceutical development, managing pharmacology, toxicology/safety and clinical development as well as CMC (chemistry, manufacturing and control)

08/2000 -

Development manager, Astion A/S (Institute of Drug Analysis A/S)

MANAGING

- Supply chain establishment i.e. global sourcing and evaluation of raw materials and manufacturers
- New product formulation incl. packaging
- Product evaluation (safety, pharmacology and clinical trials)
- Product Development
- Project management

02/1998 -

Project manager at Institute of Drug Analysis A/S, Copenhagen, a private research and development company, as well as a manufacturer (out-sourced) of unique plant-based products for the pharmaceutical, cosmetic and food industry.

GENERAL TASKS	MAIN ACHIEVEMENTS
<ul style="list-style-type: none"> • Project management • New product development • Research and development of pharmacologically active ingredients, analytical methods (HPLC/MS and GC/MS) and formulations. • Establish documentation of active principle through scientific literature and/or clinical trials in cooperation with pharmacologists and clinical research manager. • Handling contract production and raw material sourcing on international markets 	<ul style="list-style-type: none"> • Developed new herbal remedy formulation from idea to finished product through development, formulation, scale-up production (Asia) and sales. • Formulated, developed and manufactured several dermatological products incl. high-end skin care ranges and pharmaceutical formulations. • Performed dissolution testing on 8 different herbal remedy formulations. Testing bioavailability by HPLC-MS analysis of actives or

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<ul style="list-style-type: none"> sourcing on international markets. Active participation in concept development, branding, marketing and positioning strategy of new product ranges. 	<ul style="list-style-type: none"> markers. Clinical studies of increased bioavailability of selected herbal remedies incl. design, formulation, sample preparation and HPLC on human plasma.
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03/1997 - 01/1998

Analytical chemist at AB AnalyCen, a Swedish contract laboratory specialising in a broad range of analytical chemistry and control.

GENERAL TASKS	MAIN ACHIEVEMENTS
<ul style="list-style-type: none"> Project management Chemical analysis e.g. traces of aflatoxins by HPLC. Development of analytical methodology, validation and accreditation. Quality control Key account customer service. System analysis and optimisation. 	<ul style="list-style-type: none"> Validation and listing of more than 25 chemical analyses Development and validation of analytical method of astaxanthin Purchased, validated and implemented new analytical instruments e.g. atomic nitrogen analyser for protein analysis. Development and Implementation of a MS Access database of customers, chemical analysis ordered, results and prints of certificate of analysis. Designed and rebuild entire laboratory for 12 people incl. outsourcing and licensing of contract work.

1991 - 1994

<ul style="list-style-type: none"> Tutorial assistant in physical chemistry at the University of Odense. Private coach in general chemistry, organic chemistry and inorganic chemistry for medical undergraduate students at the University of Odense. Teaching assistant in mathematics and physics at The Engineering College in Odense. Trainee at KommuneKemi A/S, where practical experience was obtained in the following fields: Reception of chemical waste, analytical chemistry, the combustion of chemical waste, the treatment of inorganic chemical waste, inspection and the department of project management and maintenance.
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08/1989 - 04/1990

Royal Danish Airforce in Skrydstrup.

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COURSES AND EDUCATION:

01/2002

"Young Managers Programme"- INSEAD, France

2000 - 2001

"Business Development and Technology Assessment", Internal training by Chief Research Officer

03/2000

"Basic Rheology", Calmia, Sweden

09/1999 - 09/2000

"Cosmetic Scientist" - Diploma course at Society of Chemical Scientists, London College of Fashion.

Main focus on:

- Product formulation and development
- Production and product evaluation
- Quality control
- Marketing

1998 - 1999

- "GMP in the purchasing department", Danish College of Pharmacy Practice, Denmark
- "Patent Conditions", Ph.D. course, Research Academy, Denmark.
- "Project management 3 - control, management and results", DIEU, Danish International Training and Education, Copenhagen
- "Internet security", it-gruppen a/s, Copenhagen
- "Business Economics", Copenhagen Business College
- "Business Organisation, Human resources", Copenhagen Business College
- "General Management", Copenhagen Business College
- "System Administration", BFC Education, Denmark
- "Advanced Network Understanding", Scandinavian Technology & Trade Center, Denmark.
- "GMP workshop", internal QA.
- "GMP for small/new production companies", Danish College of Pharmacy Practice, Denmark

09/1994 - 11/1996

Master of Science degree in Chemistry from the University of Odense. Last 6 months of theses was completed at the University of Queensland, in Australia in Prof. Curt Wentrups group. Practical experience was gained in the following areas:

- General Research.
- Development of new methods in synthesis and flash vacuum pyrolysis.
- Mass Spectrometry, NMR, IR, chemical analysis etc.

08/1991 - 06/1994

Diploma degree in Chemical Engineering at The State Recognised Engineering College in Odense. Practical experience in the following areas:

- Development of method to separate mercury from contaminated waste (theses).
- Reaction kinetics and Technical Chemistry (reactor design, optimising etc.).
- Environmental Chemistry and Instrumental Analysis.